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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/766,283	01/27/2004	Bal Ram Singh	08387-002003	3757

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 08/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/766,283	SINGH ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7,17-26 and 30* is/are pending in the application.

4a) Of the above claim(s) *1,7,17-21,25,26 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/27/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group III, claims 22-24 without traverse in the Response to Restriction Requirement, filed July 24, 2006 is acknowledged. Claims 1, 7, 17-21, 25, 26 and 30 are non-elected invention and withdrawn from consideration. Therefore, claims 22-24 are examined.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 22-24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 22-24 are directed to a method of treating a patient who is suffering from a disease or condition associated with excessive release of acetylcholine from presynaptic nerve terminals, the method comprising administering to the patient a therapeutically effective amount of a polypeptide complex comprising a botulinum toxin and more than one botulinum toxin type E neurotoxin associated polypeptide. While the specification discloses type E botulinum toxin exists in a complex that includes the toxin and five other polypeptides termed neurotoxin associated proteins (NAPs) such as NAPs having molecular weights of approximately 80, 65, 40

and 18 kDa, and a method of treating patients who suffer from a disease or condition associated with excessive release of acetylcholine from presynaptic nerve terminals by administering to the patient a therapeutically effective amount of a polypeptide complex that contains botulinum toxin (or other serotype toxin) and more than one NAP, e.g., one or more the 80, 65, 40, and 18 kDa NAPs, and/or the 118 kDa neurotoxin binding protein (NBP; pages 2-3), it does not identify any fragments or variants of NAPs that have the same function as full length of NAPs with molecular weights of 80, 65, 40 and 18 kDa. The specification only discloses the 18 kDa polypeptide comprising SEQ ID NO:1, the 40 kDa polypeptide comprising SEQ ID NO:2, the 65 kDa polypeptide comprising SEQ ID NO:3, the 80 kDa polypeptide comprising SEQ ID NO:4, and the full length of the 18 kDa polypeptide being SEQ ID NO:5 (pages 14-17), and the NAPs protect the toxic activity of botulinum toxin form heat (pages 18-19), it does not describe a genus of variants for botulinum toxin type E neurotoxin associated polypeptides in the complexes, and the use of these complexes in the claimed method. A few species of type E NAPs (the polypeptides having 80, 65, 40 and 18 kDa) do not provide written description for a genus of variants of type E NAPs. Without guidance on the structure to function/activity relationship for various type E NAPs, one skilled in the art would not know which domain in the NAPs is essential for the function, and which NAP fragment or variant is functional. The lack of description on the structure to function/activity relationship for type E NAPs in the complexes used for the claimed methods and the lack of representative species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise terms that a skilled artisan would not recognize applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 22-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4. Claims 22-24 are indefinite as to what result a therapeutically effective amount of the polypeptide complex would produce in the treatment. The claims are also indefinite because of the use of the term "excessive release of acetylcholine", it is not clear what extent of release the term refers to, and what disease or condition that is associated with excessive release of acetylcholine from presynaptic nerve terminals. Claims 23-24 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

5. Claims 22-24 are indefinite because the claims are dependent from a non-elected claim, claim 1.

Conclusion

6. No claims are allowed.

Art of Record

Aoki *et al.* (WO 95/17904) disclose a method of treating a condition related to cholinergic controlled secretions including excessive sweating, lacrimation and mucous secretion, or a method of treating smooth muscle disorders such as spasms in the sphincter of the cardiovascular arteriole, gastrointestinal system, urinary, gal bladder and rectum, by

administering to a patient suffering from the disorder a therapeutically effective amount of botulinum toxin serotypes B, C, D, E, F and G (page 4, line 29-page 5, line 7), e.g., the use of botulinum toxin type E to treat tardive dyskinesia (Example 1©), spasmodic torticollis (Example 2(d)), essential tremor (Example 3©), spasmodic dysphonia (Example 4©). However, Aoki *et al.* do not disclose the use of a polypeptide complex comprising botulinum toxin type E and botulinum toxin type E neurotoxin associated polypeptide.

Singh *et al.* (J. Protein Chemistry 14, 7-18 (1995)) teach a botulinum toxin type E neurotoxin binding protein has been purified as a 118 kDa protein, which can interact with type E neurotoxin to form a complex as shown in gel filtration, where the neurotoxin binding protein can protect the neurotoxin from adverse pH, temperature and proteolytic condition (abstract). However, Singh *et al.* do not teach the polypeptide complex comprising botulinum toxin type E and more than one botulinum toxin type E neurotoxin binding protein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Primary Patent Examiner

CHIH-MIN KAM
PATENT EXAMINER

CMK
August 17, 2006